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BRACHYTHERAPY

Brachytherapy xxx (xxxx) xxx

Technical Note

A novel 3D-printed brachytherapy applicator and monte Carlo model for the treatment of conjunctival tumors

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ABSTRACT

PURPOSE: To develop a custom low dose rate brachytherapy applicator for the treatment of conjunctival malignancies which leverages 3D-printing technology to provide enhanced design flexibility and availability.

METHODS: An elliptical shell applicator inspired by ocular surgery postoperation conformer shells was developed for the placement of the applicator around the cornea of the eye, with a central hole to provide patient comfort. The applicator featured 2 concentric circles of slots for iodine-125 seeds, providing customization of the dose distribution depending on the location of the target. The applicator was modeled using computer-aided design software. The resultant model STL file was used for 3D printing of the applicator and the development of a Monte Carlo model of the applicator and its dose distribution.

RESULTS: The applicator was successfully 3D printed using biocompatible resin, which could be sterilized for treatment after manual source loading. A Geant4 model of the applicator was created directly from the STL model and was applied to a phantom to estimate the dose distribution delivered by the applicator. The toroidal dose distribution allowed for treatment of the conjunctiva while reducing dose to the cornea compared to traditional eye plaque designs.

CONCLUSIONS: A custom 3D-printed applicator was successfully developed and modeled for the treatment of conjunctival malignancies. This novel applicator design potentially provides higher quality, more customizable dose distributions for patients and the simplicity of the design makes it accessible for any clinic with 3D-printing technology.

Keywords: 3D printing; Conjunctival tumors; Eye plaques; Monte Carlo

Introduction

Localized conjunctival malignant tumors are mostly managed with the excisional biopsy of the conjunctival tumor with cryotherapy to the surrounding margins. When the tumor invades the orbit or periocular tissue, exenteration or enucleation is the primary treatment choice. When the tumor shows diffuse involvement of the conjunctival surface or invades the sclera, additional techniques have been developed to provide additional localized adjuvant therapies to improve patient outcomes. Brachytherapy has shown to be an effective method to provide adjuvant treatment to conjunctival malignancies, with well-tolerated, low-toxicity treatments.

Due to the unique nature of the location of these treatment targets, a wide variety of applicators have been utilized, with the most common being standard episcleral plaques such as COMS I-125 or Ru-106 applicators (1,2). The challenge presented using these standard plaques is that often their dose covers the entire scleral surface below the plaque, which may not be ideal in the case of conjunctival malignancy due to the tumor often presenting as a ring around the cornea, resulting in unnecessary treatment of healthy tissue. This challenge has driven interest in the development of custom applicators for the adjuvant brachytherapy of this disease.

Received 10 April 2024; received in revised form 9 July 2024; accepted 17 July 2024; Available online xxx

Disclosures: Dr. Hakan Demirci is a member of the Castle Biosciences advisory board. The other authors declare no conflicts of interest.

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1538-4721/$ - see front matter

https://doi.org/10.1016/j.brachy.2024.07.004

Attempts were made to create custom brachytherapy applicators using a custom mold or slotted gold plaque that house loose radioactive seeds to treat conjunctival malignancy by other investigators (3,4). However, these approaches lack design flexibility. In recent advancements within 3D printing technology, diverse medical applications have emerged, encompassing the creation of prototypes or the actual production of personalized surgical tools (5–7), training instruments (8), and quality assurance devices (9–11). Particularly noteworthy is the utilization of 3D printing in the development of brachytherapy applicators (12–16). Custom 3D-printed brachytherapy applicators have been especially valuable for less commonly treated brachytherapy sites, such as the nasopharynx, oral cavity, skin and intraoperative sites (17–22) . While multiple 3D printing techniques are available (23), the resin-based stereolithography printing method provides superior spatial resolution and biocompatibility, making it particularly well-suited for the production of brachytherapy applicators for seed implant. This paper introduces a pioneering design and manufacturing approach employing this resin-based 3D printing technique. The focus of this innovation is the creation of an ocular brachytherapy applicator tailored specifically for the Iodine-125 based low dose rate brachytherapy treatment of conjunctival malignancies.

Materials and methods

The conjunctival tumor brachytherapy applicator designed in this work was inspired by the plastic conformer shells placed in a patient's eye postenucleation or evisceration to maintain the shape of the eye socket and reduce swelling. The custom applicator was an elliptical shell designed to be placed directly on the conjunctiva of the eye around the cornea (Fig. 1). The applicator can be approximated as an ellipse with a major axis of 27.9 mm and a minor axis of 25.8 mm. The applicator design is curved to fit the shape of the eye in the inner portions but is flared out at the edges such that it can conform to the bulbar conjunctiva at the edges of the eye. The shell features a circular opening over the cornea to minimize discomfort and corneal ulceration during the duration of the implant (24). The applicator features slots designed for IAI-125A seeds (IsoAid, LLC, Port Richey, FL). Note that although this

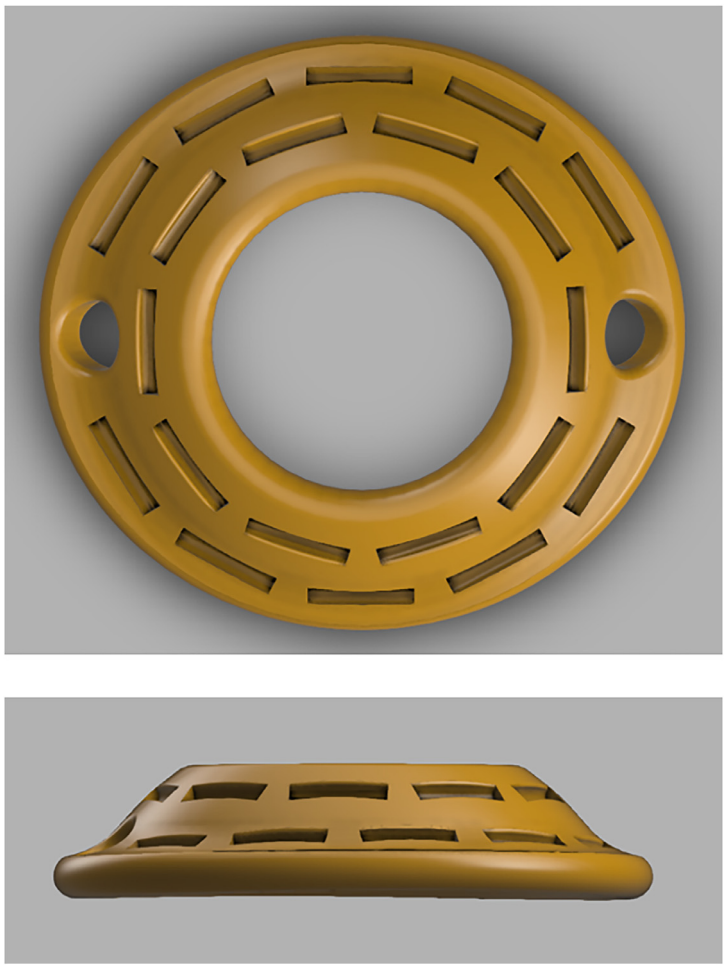

Fig. 1. A top and side view of the design of the conjunctival malignancy brachytherapy applicator created in the CAD software.

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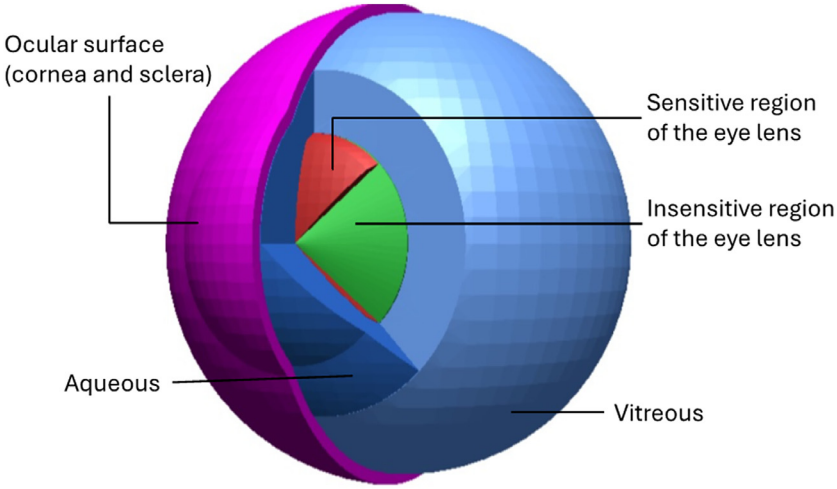

Fig. 2. Substructures of the eye lens model of the amMRCP.

applicator was specifically designed for IAI-125A seeds, it could easily be slightly modified to fit most commercially available I-125 seeds without significantly altering the proposed design since the seeds generally have very similar dimensions (25). Slots are placed in 2 concentric circles around the applicator, 10 inner slots near the inner corneal opening and 10 outer slots near the outer edge of the applicator. This multilevel design allows for the selective loading of the applicator to focus treatment on the portions proximal or distal to the cornea, creating a torus-shaped dose distribution around the applicator. Two holes are placed at the lateral and medial edges of the applicator to allow for the applicator to be directly sutured to the eye to prevent shifting after implant.

The applicator design was created using the Fusion 360 3D CAD software (Autodesk, San Fransisco, CA). The 3D model was exported as an STL file, which was imported into the Formlabs Preform application for 3D printing. A Form 3B+ (Formlabs, Boston, MA) stereolithography 3D printer was used to print the applicator with 50-micron accuracy. The applicator was printed using BioMed Clear V1 resin, which is a biocompatible resin that allows for long-term contact with mucosal membranes or skin as well as sterilization. It required approximately 1.75 hours and 3.5 ml of resin to print a single applicator. The postprocessing of the applicator included a 20-minute cleaning cycle by submerging it in 99% isopropanol and a 60-minute curing process of exposing the applicator to 405 nm UV light while at 60°C.

For the Monte Carlo particle transport simulations, the IAI-125A seed model, which was previously validated by the work of Aryal et al., was created as an STL file and precisely integrated into the centers of the slots in the 3D applicator model using Rapidform software (INUS Technology Inc., Korea) to prevent any intersections (26). Note the source geometry and source energy spectrum used in the model were provided through personal communication with the authors. The slots of the 3D applicator are slightly larger than the IAI-125A seed, which allows the seed to move ± 0.05 mm along the capsule long axis and ± 0.1 mm in lateral direction. The composite model, initially in polygonal mesh form, was transformed into a tetrahedral mesh with the POLY2TET program (27), significantly enhancing computational efficiency. This model was implemented in the Geant4 code version 11.1.3 (28), alongside the adult male Mesh-type Reference Computational Phantom (amMRCP) (29), by meticulously positioning the applicator close to the eyeball. As illustrated in Fig. 2, the eye model of amMRCP defines substructures including ocular surface (i.e., cornea and sclera) and eye lens. Note that the eye lens is subdivided to specifically represent sensitive region where the epithelial cells are mostly distributed. The models were incorporated using the G4VUserParallelWorld class, allowing for geometry overlap with the phantom but giving priority to the applicator and seed models in overlapping regions. The dose distribution was determined using built-in scoring mesh function of Geant4, set to a grid size of $0.2 \times 0.2 \times 0.2$ mm^3 and a resolution of $300 \times 300 \times 300$. Primary photons, uniformly emitted from the IAI-125A source's I-125 coating, were simulated using the G4VUserPrimaryGeneratorAction class, with photon and electron transported with the G4EmLivermorePhysics library by applying the secondary production cut of 1 μm. A total of 3.4×10^9 particles were transported to maintain statistical relative errors for the absorbed doses to tissue lower than 0.1% and a low statistical relative error across the grid, and no variance reduction techniques were employed. The absorbed doses to tissue were calculated both as dose-to-medium-in-medium and as dose-to-water-in-water, the latter being converted from dose-to-medium-in-medium using Bragg-Gray cavity theory (30,31).

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Table 1
Absorbed doses per seed-specific disintegration calculated for left eye lens, its sensitive region, and ocular surface of the left eye (unit: $pGy \cdot s^{-1} \cdot Bq^{-1}$) alongside with the statistical errors for Monte-Carlo method.

Tissue	Dose-to-medium-in-medium	Dose-to-water-in-water	Statistical error
Eye lens	0.050	0.051	0.04%
Sensitive region of eye lens	0.054	0.055	0.10%
Ocular surface (cornea and sclera)	0.041	0.041	0.02%

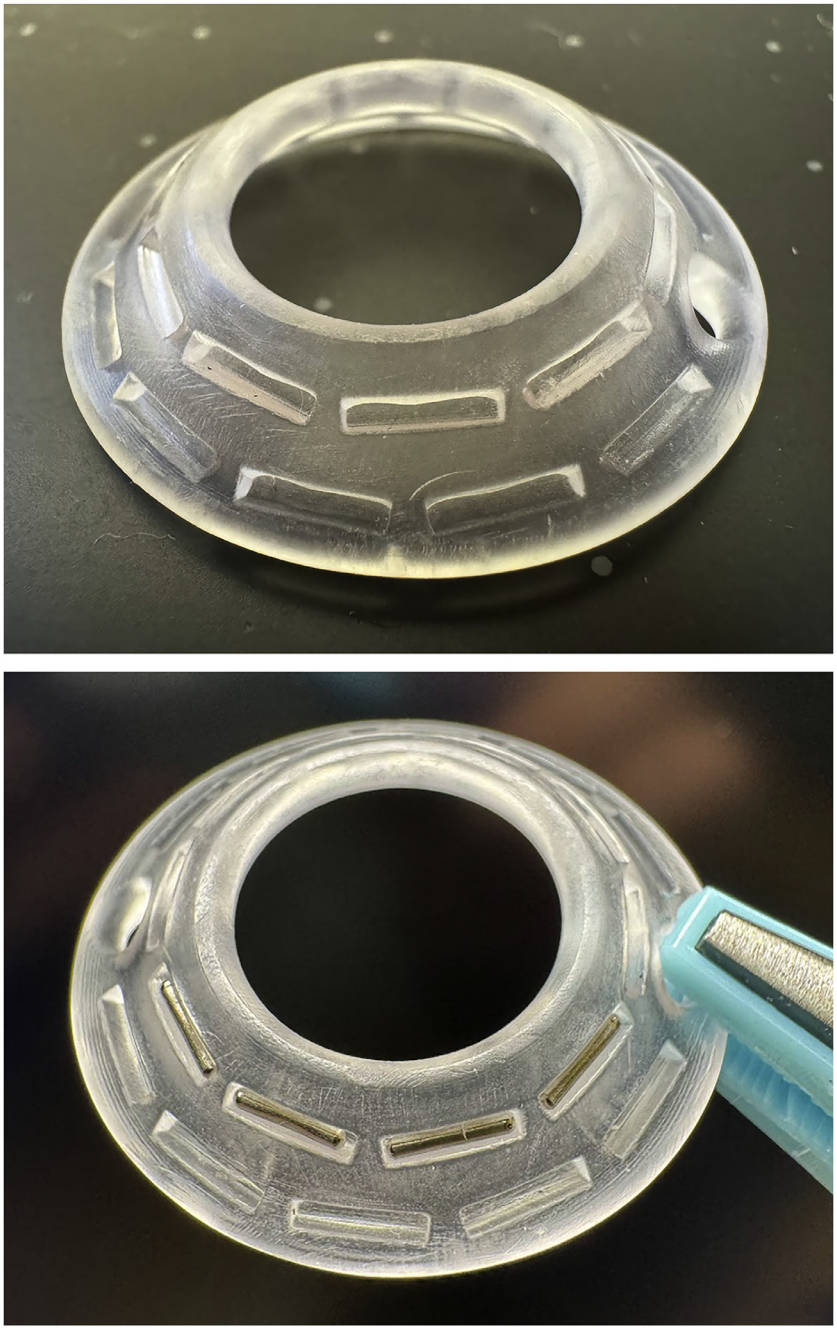

Fig. 3. The applicator after 3D printing with and without dummy seeds in place.

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Results

The applicator was successfully printed and postprocessed to result in geometric precision adequate for the insertion of dummy IAI-125A seeds. The applicator was easily assembled by immobilizing the seeds in the slots via medical grade RTV silicone. It was found that the biocompatible resin was smooth enough after post processing to be placed comfortably in the eye. The completed applicator before loading and loaded with dummy seeds are shown in Fig. 3.

Table 1 shows the absorbed doses per seed-specific disintegration calculated for the left eye lens, its sensitive region, and the ocular surface of the left eye, in both dose-to-medium-in-medium and dose-to-water-in-water. It can be seen that the statistical errors are lower than 0.1%. For all tissues, dose-to-water-in-water was approximately 1% larger, which is due to the slightly higher stopping power in the tissue materials. Figure 4 displays the model of the IAI-125A seeds and applicator positioned on the left eye of the amMRCP, along with the dose distributions calculated by the Geant4 code for the coronal, sagittal, and transverse

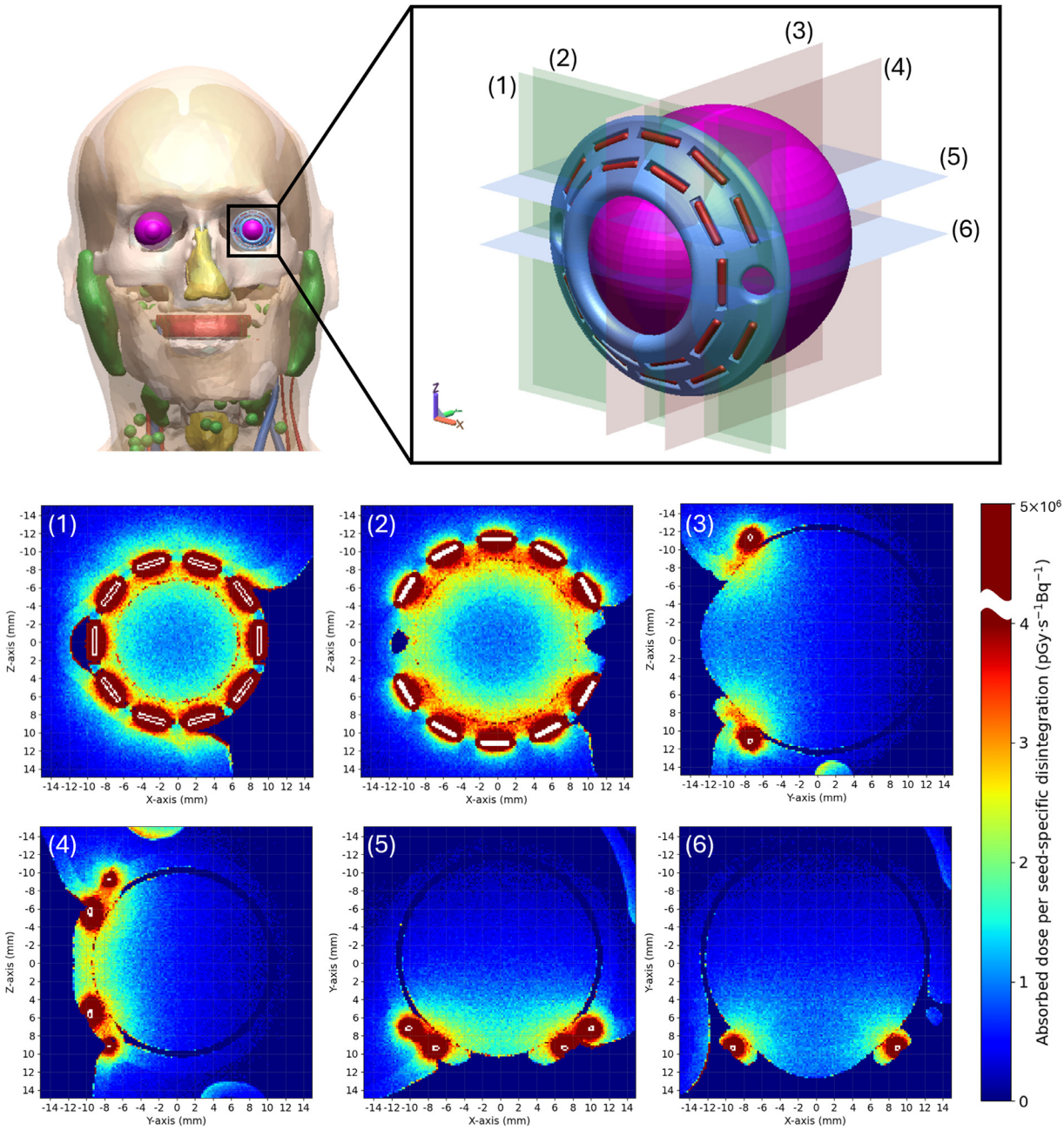

Fig. 4. Dose distributions calculated by Geant4 code displayed for coronal, sagittal, and transverse planes.

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planes. The figure illustrates that the seed and applicator models were precisely installed just above the eyeball. For the visualization of dose distributions through heat maps, areas receiving a dose exceeding 5 $\mu Gy \cdot s^{-1} \cdot Bq^{-1}$ are highlighted in white, primarily representing the region around the I-125 coating of the IAI-125A source. The center of the eyeball was set as the origin for these heat maps.

The applicator could be sterilized either by the standard antiseptic solution or through the steam sterilization before treatment. Insertion procedure for the applicator could be performed similarly to a standard COMS eye plaques by an ophthalmologist in an operating room and sutured directly to the patient's eye. A leaded eye patch could be placed over the eye for radiation protection for individuals around the patient.

Discussion

In this study, we designed a brachytherapy applicator specifically for the adjuvant radiation treatment of conjunctiva malignancies. One major advantage of this approach over a traditional COMS plaque is the location of the activity within the applicator. COMS plaques are arranged such that the dose distribution focuses the dose at a focal point along the central axis of the plaque, resulting in a dose distribution of relatively uniformly arced isodose lines spreading from the front of the plaque (32). Although this is desirable in the case of a solid ocular tumor, in cases of conjunctival malignancies where residual disease is spread in a concentric circle adjacent to the cornea, this may result in unnecessary dose to healthy tissues in the cornea, iris, and lens. The applicator presented in this study provides a torus-shaped dose distribution that focuses dose to both the bulbar and palpebral conjunctiva without causing unnecessary dose to cornea. This applicator can also be easily selectively loaded to focus the dose distribution to only treat a portion of the conjunctiva to further contain the dose to the target regions.

Another advantage of the applicator presented in this work over tradition COMS plaques is in their manufacturing. The use of 3D printing has been shown in the literature as a cost-efficient way to produce custom medical devices efficiently, especially in times of supply chain issues (33,34). This is also the case with the presented applicator, which could be manufactured in a matter of hours in-house relatively cheaply. The only additional materials that still require ordering from the manufacturer are the I-125 seeds for the applicator.

Although the applicator presented in this work provides some distinct advantages in the treatment of conjunctival malignancies, it does have some drawbacks. First, the current design does not provide the option of only treating the bulbar or palpebral conjunctiva due to the lack of shielded backing in the design. Work in developing this option is currently ongoing and would likely require the addition of thin metal shielding attachments to either side of the applicator to selectively spare the bulbar or palpebral conjunctiva while still fitting in the patient's eye. The other drawback in the current work is that the model assumes the applicator is radiologically equivalent to water. The current effect of the 3D-printed plastic on the dose distribution when compared to a water is not accounted for and further investigation through Monte Carlo could be warranted. This has not been done to date since the makeup of the applicator resin is proprietary. Also, it is important to note that previously presented iterations of this applicator design have been used to treat a small number of patients successfully and safely, the presented applicator design requires further clinical application to establish its effectiveness (35–37).

Conclusions

The design and Monte Carlo dose calculation for a 3D-printed I-125 brachytherapy applicator for the treatment of conjunctival malignancies was described. This applicator results in a torus-shaped dose distribution that focuses dose to the surface of the conjunctiva adjacent to the cornea while reducing unnecessary dose to the cornea and other structures of the eye. The customizability and simplicity of the design of this applicator through the use of 3D-printing should make it accessible other clinics treating conjunctival malignancies with COMS plaques that have 3D-printing capability. Overall, this applicator design could potentially provide a higher quality, more customized treatment to a subset of conjunctival malignancy patients that are underserved by the traditional COMS eye plaque design.

Acknowledgments

We would like to thank Kwok Lam for inspiration and valuable discussion during the initial design stages of the applicator. We also wish to thank Mark Rivard for providing source information about the I-125 seeds to assist in creating the Monte Carlo model.

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